



## Effect of Vitamin Intervention on the Relationship between GSTM1, Smoking, and Lung Cancer Risk Among Male Smokers

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**Abstract:** The GSTM1 (glutathione S-transferase mu-1) null genotype is suspected of increasing an individual's susceptibility to tobacco smoke carcinogens because of impaired carcinogen detoxification. We were interested in whether there were differences in lung cancer susceptibility to smoking within the GSTM1 genotypes and the impact of antioxidant supplementation on this. For this purpose, we conducted a nested lung cancer case-control study and evaluated the role of GSTM1 within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. GSTM1 genotype status was determined for 319 cases and 333 controls using a PCR based approach. GSTM1 was evaluated as an independent risk factor and as an effect modifier of smoking using logistic regression analyses. The GSTM1 null genotype itself was unrelated to risk of lung cancer, odds ratio (OR) = 1.09 and 95% confidence interval (CI), 0.79-1.50, but it may have modified the effect of smoking. There was a suggestion for a stronger association between years of smoking and lung cancer among the GSTM1 null genotype, but the differences between GSTM1 null and present genotypes were not statistically significant ( $P = 0.12$ ). Furthermore, the smoking association was strongest among those with the GSTM1 null genotype not receiving alpha-tocopherol supplementation, whereas among those receiving alpha-tocopherol, there was no modification by GSTM1 on the association between smoking duration and lung cancer risk. beta-Carotene supplementation did not modify the relationship between GSTM1, smoking years, and lung cancer risk. In conclusion, GSTM1 is not associated with lung cancer risk in male smokers but may confer a higher susceptibility to cumulative tobacco exposure. This association may be attenuated by alpha-tocopherol but not by beta-carotene supplementation.